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NEWS 14 FEB 22 Updates in EPFULL; IPC 8 enhancements added
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NEWS 22 MAR 22 EMBASE is now updated on a daily basis
NEWS 23 APR 03 New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS 24 APR 03 Bibliographic data updates resume; new IPC 8 fields and IPC
thesaurus added in PCTFULL

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15562 CYCLOSPORIN
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=> HBV
8751 HBV
60 HBVS
L2 8767 HBV
(HBV OR HBVS)

=> L1 and L2
L3 10 L1 AND L2

=> CsA
8788 CSA
100 CSAS
L4 8837 CSA
(CSA OR CSAS)

=> L4 and L2
L5 8 L4 AND L2

=> BAPTA and L2
2980 BAPTA
1 BAPTAS
2981 BAPTA
(BAPTA OR BAPTAS)
L6 1 BAPTA AND L2

=> "IL2" and L2
2719 "IL2"
L7 15 "IL2" AND L2

=> nefedipine and L2
35 NEFEDIPINE
L8 0 NEFEDIPINE AND L2

=> D L5 IBIB ABS 1-8

L5 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1052150 CAPLUS

DOCUMENT NUMBER: 144:100590

TITLE: Long-term beneficial effect of tacrolimus conversion on renal transplant recipients

AUTHOR(S): Lee, Wen-Chin; Lian, Jong-Da; Wu, Ming-Ju; Cheng, Chi-Hung; Chen, Cheng-Hsu; Shu, Kuo-Hsiung

CORPORATE SOURCE: Division of Nephrology, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan

SOURCE: Renal Failure (2005), 27(5), 501-506

CODEN: REFAE8; ISSN: 0886-022X

PUBLISHER: Taylor & Francis, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Objective. Acute rejection, chronic allograft nephropathy, and cyclosporine (**CsA**) toxicity remain serious problems for renal transplant recipients and may lead to graft loss. We retrospectively analyzed 34 patients whose biopsies revealed acute and/or chronic allograft rejection, or **CsA** nephrotoxicity, and who converted from **CsA** to tacrolimus. Patients and Methods. From July 1996 through Sept. 2003, **CsA** was converted to tacrolimus in 34 renal transplant recipients (26 male, 8 female) with renal biopsy at our hospital. Blood pressure and serum creatinine levels were checked monthly and serum cholesterol, triglyceride, and glutamic-pyruvic transaminase (GPT) levels were checked every three months. Results. A consistently stable and better function after conversion was obtained in a significant portion (24, 71%) of patients. A statistically significant decline in serum creatinine and an improvement in the glomerular filtration rate were found at 3 m, 6 m, 12 m, 36 m, and 72 m after tacrolimus conversion. In 85.7% (12/14) of patients with acute rejection and in 35.7% (5/14) of patients with chronic allograft nephropathy (concomitant with acute rejection in 5), improved or stabilized graft function was noted. In addition, the systolic blood pressure and diastolic BP dropped significantly ($P<0.05$), while there was no significant change in cholesterol, triglyceride, and GPT levels. Conclusion. The beneficial effect of tacrolimus conversion on patients with acute rejection, chronic allograft nephropathy, or **CsA** nephrotoxicity was demonstrated in long-term follow up. The improvement in both renal function and blood pressure may be of paramount importance in reducing long-term cardiovascular morbidity and mortality.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:271102 CAPLUS

DOCUMENT NUMBER: 142:422884

TITLE: Inhibitory effect of cyclosporine A on hepatitis B virus replication in vitro and its possible mechanisms

AUTHOR(S): Xia, Wei-Liang; Shen, Yan; Zheng, Shu-Sen

CORPORATE SOURCE: Department of Hepatobiliary Surgery, First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, 310003, Peop. Rep. China

SOURCE: Hepatobiliary & Pancreatic Diseases International (2005), 4(1), 18-22

CODEN: HPDIAJ; ISSN: 1499-3872

PUBLISHER: First Affiliated Hospital, Zhejiang University School of Medicine

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. BACKGROUND: Hepatitis B related end-stage liver disease is recently acknowledged as one of the main indications for orthotopic liver transplantation (OLT). However, the high recurrence rate of hepatitis B virus infection following transplantation is regarded as a major factor affecting the long-term survival of transplant recipients especially in China. Cyclosporine A (**CsA**), which is routinely used to prevent the allograft rejection, is reported to have the inhibitory activity on

hepatitis B virus (HBV) replication in vitro. In this paper, we review the inhibitory effect and its possible mechanisms of **CsA** on HBV replication in vitro. DATA RESOURCES: An English-language literature search was conducted using MEDLINE (1990-2004) on cyclosporine A, hepatitis B virus, mitochondria, calcium and other related reports and review articles. RESULTS: Hepatitis B x protein (HBx) is essential to HBV replication. The cytosolic calcium signaling mediated by mitochondria and the Src kinase pathway were involved during HBx activation of HBV replication. **CsA** inhibits the HBV replication in vitro by its binding to mitochondrial cyclophilin D, then blocking the mitochondria-mediated cytosolic calcium signaling. The derivatives of **CsA** also have the HBV replication inhibitory effect in vitro. CONCLUSIONS: By interacting with mitochondria, preventing the release of intramitochondrial calcium, and then blocking the cytosolic calcium signaling, **CsA** inhibits the HBV replication in vitro. The derivatives of **CsA** also have this activity.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:67524 CAPLUS
DOCUMENT NUMBER: 142:312974
TITLE: Calcium ions affect the Hepatitis B virus core assembly
AUTHOR(S): Choi, Yongwook; Park, Sung Gyoo; Yoo, Jun-Hi; Jung, Guhung
CORPORATE SOURCE: School of Biological Sciences, Seoul National University, Seoul, 151-742, S. Korea
SOURCE: Virology (2005), 332(1), 454-463
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previous report showed that cytosolic Ca²⁺ induced by hepatitis B virus X protein (HBx) promotes HBV replication. In this study, in vitro expts. showed that (i) HBV core assembly in vitro was promoted by Ca²⁺ through the sucrose d. gradient and the anal. ultracentrifuge anal. Also, (ii) transmission electron microscope anal. demonstrated these assembled HBV core particles were the capsids. Ex vivo expts. showed that the treatment of BAPTA-AM and cyclosporine A (**CsA**) reduced HBV capsids in the transfected HepG2 cells. In addition to that, the treatment of Thapsigargin (TG) increased HBV capsids in the transfected HepG2 cells. Furthermore, we investigated the increased HBV core assembly by HBx. The results show that the increased cytosolic calcium ions by HBx promote the HBV core assembly.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:60754 CAPLUS
Correction of: 2004:1036571
DOCUMENT NUMBER: 142:233342
Correction of: 142:16836
TITLE: Sequences of human schizophrenia related genes and use for diagnosis, prognosis and therapy
INVENTOR(S): Liew, Choong-Chin
PATENT ASSIGNEE(S): Chondrogene Limited, Can.
SOURCE: U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S. Ser. No. 802,875.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 29
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 2004241727	A1	20041202	US 2004-812731	20040330
US 2004014059	A1	20040122	US 2002-268730	20021009
US 2005191637	A1	20050901	US 2004-803737	20040318
US 2005196762	A1	20050908	US 2004-803759	20040318
US 2005196763	A1	20050908	US 2004-803857	20040318
US 2005196764	A1	20050908	US 2004-803858	20040318
US 2005208505	A1	20050922	US 2004-803648	20040318
US 2004265869	A1	20041230	US 2004-812716	20040330
US 2005208519	A1	20050922	US 2004-989191	20041115

PRIORITY APPLN. INFO.:

US 1999-115125P	P	19990106
US 2000-477148	B1	20000104
US 2002-268730	A2	20021009
US 2003-601518	A2	20030620
US 2004-802875	A2	20040312
US 2004-812731	A2	20040330
WO 2004-US20836	A2	20040621

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing and monitoring diseases using gene-specific and/or tissue-specific primers. The present invention also describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of 3 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L5 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:126759 CAPLUS

DOCUMENT NUMBER: 139:270546

TITLE: Single-center experience: tacrolimus and mycophenolate mofetil in early stage of kidney transplantation with liver dysfunction

AUTHOR(S): Liu, B.; Lin, Z. B.; Zeng, F. J.; Ming, C. S.; Sha, B.; Chen, Z. S.; Chen, S.

CORPORATE SOURCE: Tongji Medical College, Tongji Hospital, The Institute of Organ Transplantation, Huazhong University of Science and Technology, Wuhan, Peop. Rep. China

SOURCE: Transplantation Proceedings (2003), 35(1), 273-274
CODEN: TRPPA8; ISSN: 0041-1345

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Although 1-yr patient survival rates in kidney transplantation has increased to 95 % in China, little further improvement has been achieved recently. Hepatic failure, sepsis, and cardiovascular complications are the leading causes of death instead of chronic allograft nephropathy. Chronic viral hepatitis infection and drug-induced toxicity increase the risk of hepatic failure. About 20 % Chinese are hepatitis B virus (HBV) carriers. Many patients suffering from end-stage renal disease are simultaneously infected with hepatitis virus, which was considered a contraindication to kidney transplantation half a decade ago. Since the conventional immunosuppressive agents cyclosporine (CsA) and azathioprine (Aza) display hepatic side effects, they can hardly be included in the immunosuppressive protocol. It has been suggests that liver function is less influenced by tacrolimus (FK506) or mycophenolate mofetil (MMF), and they may have a potential role in therapy for kidney allograft recipients with liver dysfunction. The present single-center study evaluated the efficacy and safety of FK506 in combination with MMF in these high-risk patients. The tacrolimus and MMF combination as primary immunosuppressants were well tolerated in kidney transplant recipients with liver dysfunction through the induction phase, neither worsening liver damage nor increasing the incidence of acute rejection. Their impact on hepatitis virus reactivation in stable patients is under investigation.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:725172 CAPLUS
DOCUMENT NUMBER: 137:261548
TITLE: Adoptive transfer of **HBV** immunity by kidney
transplantation and the effect of postoperative
vaccination
AUTHOR(S): Dahmen, Uta; Gu, Yanli; Dirsch, Olaf; Li, Jun;
Polywka, Susanne; Doebel, Lothar; Shen, Kai; Broelsch,
Christoph Erich
CORPORATE SOURCE: Department of General and Transplantation Surgery,
University Hospital Essen, Essen, Germany
SOURCE: Antiviral Research (2002), 56(1), 29-37
CODEN: ARSRDR; ISSN: 0166-3542
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Transfer of hepatitis B immunity occurs upon the transfer of immunol.
active cells from the donor to the recipient by means of an organ graft.
This has been repeatedly demonstrated for bone marrow and liver
transplantation. Evidence is now presented for the transfer of
anti-hepatitis B surface antibodies (anti-HBs) after kidney
transplantation in rats. Kidney donors from one syngeneic and two
allogeneic rat strains were immunized twice with 4 µg of recombinant
hepatitis B vaccine. In week 6 after the first vaccination, kidney grafts
were transplanted into Lewis (LEW) rats. Half of the recipients underwent
daily immunosuppressive treatment with cyclosporin A (**CsA**). All
recipients were vaccinated either after 10 wk or 1 wk postoperatively.
Anti-HBs titer was measured weekly. Effective anti-HBs titers (10-227
mIU/mL, lasting for 1-7 wk) were detected in 86% (25/29) of recipient
rats, whose corresponding donors all had a titer above 15,000 mIU/mL.
Immunosuppression enhanced the donor-derived immunity in terms of
recipient-to-donor titer ratio, maximal titer and titer persistence.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:699548 CAPLUS
DOCUMENT NUMBER: 136:2662
TITLE: Nuclear factor of activated T cells (NFAT1-C)
represses the enhancer II and pregenomic promoter
(EnII/Cp) of hepatitis B virus (**HBV**) through
its responsive site GGAGA and nullifies the HBx-driven
transcriptional activation
AUTHOR(S): Lee, Joong Hyuk; Rho, Hyune Mo
CORPORATE SOURCE: School of Biological Sciences, Seoul National
University, Seoul, 151-742, S. Korea
SOURCE: IUBMB Life (2001), 51(4), 255-261
CODEN: IULIF8; ISSN: 1521-6543
PUBLISHER: Taylor & Francis
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The immunosuppressant cyclosporin A (**CsA**)-sensitive nuclear
factor of activated T cells 1 (NFAT1) has been known to be a
transcriptional regulator of cytokine and viral genes during the immune
response. By analyses of serial deletion, mutation, and heterologous
promoter assay, the authors report here that the **CsA**-sensitive
NFAT1-C represses the transcriptional activity of enhancer II and
pregenomic promoter (EnII/Cp) of **HBV** through the NFAT1-C
responsive site (GGAGA, nt 1603-1618) and nullifies the HBx-driven
transcriptional activation of the EnII/Cp of **HBV** in a
dose-dependent manner. These results suggest that a **CsA**-
sensitive NFAT1-C may control the viral activity in **HBV**-
infected cells by inhibiting the EnII/Cp and nullifying the HBx-driven
transcriptional activation.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:710042 CAPLUS

DOCUMENT NUMBER: 123:132330
TITLE: Effect of immunosuppressive and antiviral agents on hepatitis B virus replication in vitro
AUTHOR(S): McMillan, Janine S.; Shaw, Tim; Angus, Peter W.; Locarnini, Stephen A.
CORPORATE SOURCE: Victorian Infectious Diseases Reference Laboratory, Fairfield Hospital, Fairfield, 3078, Australia
SOURCE: Hepatology (Philadelphia) (1995), 22(1), 36-43
CODEN: HPTLD9; ISSN: 0270-9139
PUBLISHER: Saunders
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hepatitis B virus (HBV) DNA-transfected hepatoma cells were incubated with the immunosuppressive agents prednisolone, azathioprine, and cyclosporin A (CsA) and the antiviral agents ganciclovir and foscarnet to investigate the effects of these compds. on HBV replication. Prednisolone and azathioprine increased intracellular viral DNA and RNA levels approx. twofold and fourfold, resp. Treatment with CsA did not alter the levels of viral RNA or DNA. A combination of all three immunosuppressive agents increased the level of intracellular viral DNA eightfold, indicating an additive effect. Incubation of the cells in the presence of foscarnet decreased levels of both single-stranded and relaxed circular viral DNA, and in the presence of ganciclovir decreased the levels of relaxed circular viral DNA, predictable effects from their known mechanism of action. The stimulatory effect on viral replication induced by the combination of immunosuppressive agents was substantially inhibited by ganciclovir-foscarnet treatment. These observations could have implications for the management of recurrent HBV infection after liver transplantation.

=> D L3 IBIB ABS 1-10

L3 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1020185 CAPLUS
DOCUMENT NUMBER: 144:142373
TITLE: Steroid-Free Living-Donor Liver Transplantation in Adults
AUTHOR(S): Marubashi, Shigeru; Dono, Keizo; Amano, Koji; Hama, Naoki; Gotoh, Kunihito; Takahashi, Hidenori; Hashimoto, Kazuhiko; Miyamoto, Atsushi; Takeda, Yutaka; Nagano, Hiroaki; Umeshita, Koji; Monden, Morito
CORPORATE SOURCE: Department of Surgery and Clinical Oncology, Graduate School of Medicine, Osaka University, Suita, Osaka, Japan
SOURCE: Transplantation (2005), 80(5), 704-706
CODEN: TRPLAU; ISSN: 0041-1337
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To examine the benefits of steroid avoidance in adult living donor liver transplantation, we compared the clin. courses of nine recipients receiving basiliximab or daclizumab and 13 historical patients who received steroids. The 1-yr patient and graft survival and the incidence of acute cellular rejection were similar in both groups. The side effects of immunosuppression tended to be more frequent in the steroid group. Hepatitis C virus (HCV)-RNA levels measured early after transplantation remained suppressed in the steroid-free group. Steroid avoidance was beneficial in the recipients, as both steroid side effects and recurrence of HCV could be avoided.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:464808 CAPLUS
DOCUMENT NUMBER: 143:278717
TITLE: Immunosuppression Withdrawal After Auxiliary Liver

Transplantation for Acute Liver Failure

AUTHOR(S): Girlanda, R.; Vilca-Melendez, H.; Srinivasan, P.;
Muiesan, P.; O'Grady, J. G.; Rela, M.; Heaton, N. D.
CORPORATE SOURCE: Liver Transplant Surgical Service, London, UK
SOURCE: Transplantation Proceedings (2005), 37(4), 1720-1721
CODEN: TRPPA8; ISSN: 0041-1345
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: The potential for immunosuppression withdrawal is the rationale for auxiliary liver transplantation (AUX) in patients with acute liver failure (ALF). Patients and methods: Forty-four AUX were performed in 28 adults and 16 children with ALF secondary to seroneg. hepatitis (n = 20; 45%), paracetamol hepatotoxicity (n = 14; 32%), acute viral hepatitis (hepatitis B virus [HBV] n = 3, Epstein-Barr virus n = 1; 9%), drug-induced hepatitis (n = 3; 7%), autoimmune hepatitis (n = 2; 5%), and mushroom poisoning (n = 1; 2%). All patients fulfilled the King's College Hospital transplant criteria for ALF. After partial hepatectomy, 38 patients received a segmental auxiliary graft and six, a whole auxiliary graft. Immunosuppression was based on calcineurin inhibitors and steroids. Results: Thirty-four patients (77%) are alive after a median follow-up of 30 mo (range 4 to 124). Eight adults and two children died of sepsis (n = 6; 14%) at a median interval of 30 days (range 2 to 66), intraoperative cardiac failure (n = 1), brain edema on postoperative day 8 (n = 1), sudden death on day 35 (n = 1), and multiple organ failure associated with HBV recurrence 4 years after transplantation (n = 1). Three patients underwent retransplantation for small-for-size graft syndrome with sepsis on postoperative day 15 (n = 1) and for ductopenic rejection 4 and 15 mo after AUX (n = 2). In 10/31 (32%) survivors (6/18 adults and 4/13 children) immunosuppression was completely withdrawn after a median of 19 mo. Conclusion: Complete immunosuppression withdrawal can be achieved in a significant proportion of patients after AUX for ALF.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:923144 CAPLUS
DOCUMENT NUMBER: 139:374590
TITLE: Use of prophylactic lamivudine and mycophenolate
mofetil in renal transplant recipients with chronic
hepatitis B infection
AUTHOR(S): Lau, S. C.; Tse, K. C.; Lai, W. M.; Chiu, M. C.
CORPORATE SOURCE: Department of Paediatrics and Adolescent Medicine,
Princess Margaret Hospital, Hong Kong
SOURCE: Pediatric Transplantation (2003), 7(5), 376-380
CODEN: PETRF6; ISSN: 1397-3142
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Chronic HBsAg carriers are known to have a higher risk of hepatitis-related mortality and morbidity when undergoing kidney transplantation. Immunosuppressants might flare up the infection that could be fulminating. Lamivudine and mycophenolate mofetil (MMF) have been shown to be effective in inhibiting replication of hepatitis B virus (HBV). With these two drugs, hepatitis related adverse outcome might be preventable when these patients are being transplanted. Four Chinese adolescents with chronic HBV infection were transplanted in our Department from 1999 to 2001. Immunosuppressants included prednisolone, cyclosporin A and MMF; azathioprine was not used for its potentially liver toxic effect. Prophylactic lamivudine 3 mg/kg and maximum 100 mg daily was given just before transplantation and was continued afterwards. HBV status and liver enzymes were monitored serially. Patients were followed up for 26.0 ± 10.3 (11-34) months post-transplant and no mortality was reported. All grafts were functioning and no rejection was noted. MMF and lamivudine were well tolerated. Alanine transaminase was only transiently elevated in the first 2 mo post-transplant in all patients and became normal afterwards. The patients were clin. well and liver function was normal at the last follow-up. However, HBV DNA became pos. in three patients after

the transplantation. YMDD mutant **HBV** was neg. in one patient and undeterminable in the other three due to low virus load. In summary, with prophylactic lamivudine and MMF, short-term follow-up showed that renal transplant might be feasible and safe in chronic **HBV** carriers.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:725172 CAPLUS

DOCUMENT NUMBER: 137:261548

TITLE: Adoptive transfer of **HBV** immunity by kidney transplantation and the effect of postoperative vaccination

AUTHOR(S): Dahmen, Uta; Gu, Yanli; Dirsch, Olaf; Li, Jun; Polywka, Susanne; Doebel, Lothar; Shen, Kai; Broelsch, Christoph Erich

CORPORATE SOURCE: Department of General and Transplantation Surgery, University Hospital Essen, Essen, Germany

SOURCE: Antiviral Research (2002), 56(1), 29-37

CODEN: ARSRDR; ISSN: 0166-3542

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Transfer of hepatitis B immunity occurs upon the transfer of immunol. active cells from the donor to the recipient by means of an organ graft. This has been repeatedly demonstrated for bone marrow and liver transplantation. Evidence is now presented for the transfer of anti-hepatitis B surface antibodies (anti-HBs) after kidney transplantation in rats. Kidney donors from one syngeneic and two allogeneic rat strains were immunized twice with 4 µg of recombinant hepatitis B vaccine. In week 6 after the first vaccination, kidney grafts were transplanted into Lewis (LEW) rats. Half of the recipients underwent daily immunosuppressive treatment with **cyclosporin A** (CsA). All recipients were vaccinated either after 10 wk or 1 wk postoperatively. Anti-HBs titer was measured weekly. Effective anti-HBs titers (10-227 mIU/mL, lasting for 1-7 wk) were detected in 86% (25/29) of recipient rats, whose corresponding donors all had a titer above 15,000 mIU/mL. Immunosuppression enhanced the donor-derived immunity in terms of recipient-to-donor titer ratio, maximal titer and titer persistence.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:334594 CAPLUS

DOCUMENT NUMBER: 137:41290

TITLE: Lamivudine treatment for acute exacerbation of hepatitis B in patients undergoing immunosuppressive therapy

AUTHOR(S): Kanai, Naoko; Hasegawa, Kiyoshi; Ogawa, Miho; Naritomi, Takuma; Hayashi, Naoaki

CORPORATE SOURCE: Department of Medicine, Tokyo Women's Medical University, Tokyo, 162-8666, Japan

SOURCE: Hepatology Research (2002), 22(3), 223-230

CODEN: HPRSFM; ISSN: 1386-6346

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Lamivudine was administrated to six patients with acute exacerbation of hepatitis B who were undergoing immunosuppressive therapy. All patients had chronic hepatitis B and were receiving immunosuppressive therapy for other primary diseases (hematol. malignancies, collagen diseases, renal transplantation) when the hepatitis flared up. Only one patient tested pos. for the hepatitis B virus e (HBe) antigen. All patients had normal ALT levels and were anti-HBe-pos. before immunosuppressive therapy. The patients were treated with 150 mg of lamivudine daily. Lamivudine was well tolerated and showed no effect on the primary disease. In all patients, hepatitis B virus (**HBV**) DNA levels decreased in response to lamivudine administration. Four patients recovered from

exacerbation, but two patients died from complications. Mol. anal. revealed that, regardless of whether patients had the wild **HBV** genotype or mutations within the core promoter or precore **HBV** regions, the effectiveness of lamivudine therapy was the same. These results demonstrated that lamivudine is very effective for treating acute exacerbation of chronic hepatitis B that occurs while a patient is undergoing immunosuppressive therapy, regardless of the phenotype of the virus.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:294165 CAPLUS

DOCUMENT NUMBER: 136:304036

TITLE: Inhibition of the Src kinase family pathway as a method of treating **HBV** infection and hepatocellular carcinoma

INVENTOR(S): Schneider, Robert J.; Klein, Nicola

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 37 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002045191	A1	20020418	US 2001-955006	20010917
PRIORITY APPLN. INFO.:			US 2000-232892P	P 20000915

AB The present invention relates to therapeutic protocols and pharmaceutical compns. designed to target HBx mediated activation of Src kinase, members of the Src tyrosine kinase family and components of the Src kinase family signal transduction pathways for the treatment of **HBV** (hepatitis B virus) infection and related disorders and diseases, such as hepatocellular carcinoma (HCC). The invention further relates to pharmaceutical compns. for the treatment of **HBV** infection targeted to HBx and its essential activities required to sustain **HBV** replication. The invention is based, in part, on the Applicants' discovery that activation of Src kinase signaling cascades play a fundamental role in mammalian hepadnavirus replication. Applicants have demonstrated that HBx mediates activation of the Src family of kinases and that this activation is a critical function provided by HBx for mammalian hepadnavirus replication.

L3 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:699548 CAPLUS

DOCUMENT NUMBER: 136:2662

TITLE: Nuclear factor of activated T cells (NFAT1-C) represses the enhancer II and pregenomic promoter (EnII/Cp) of hepatitis B virus (**HBV**) through its responsive site GGAGA and nullifies the HBx-driven transcriptional activation

AUTHOR(S): Lee, Joong Hyuk; Rho, Hyune Mo

CORPORATE SOURCE: School of Biological Sciences, Seoul National University, Seoul, 151-742, S. Korea

SOURCE: IUBMB Life (2001), 51(4), 255-261

CODEN: IULIF8; ISSN: 1521-6543

PUBLISHER: Taylor & Francis

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The immunosuppressant **cyclosporin A** (CsA)-sensitive nuclear factor of activated T cells 1 (NFAT1) has been known to be a transcriptional regulator of cytokine and viral genes during the immune response. By analyses of serial deletion, mutation, and heterologous promoter assay, the authors report here that the CsA-sensitive NFAT1-C represses the transcriptional activity of enhancer II and pregenomic promoter (EnII/Cp) of **HBV** through the NFAT1-C responsive site (GGAGA, nt 1603-1618) and nullifies the HBx-driven transcriptional

activation of the EnII/Cp of **HBV** in a dose-dependent manner.

These results suggest that a CsA-sensitive NFAT1-C may control the viral activity in **HBV**-infected cells by inhibiting the EnII/Cp and nullifying the HBx-driven transcriptional activation.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:29452 CAPLUS

DOCUMENT NUMBER: 130:195699

TITLE: The hepatitis B virus X protein activates nuclear factor of activated T cells (NF-AT) by a **cyclosporin A**-sensitive pathway

AUTHOR(S): Lara-Pezzi, Enrique; Armesilla, Angel Luis; Majano, Pedro L.; Redondo, Juan Miguel; Lopez-Cabrera, Manuel

CORPORATE SOURCE: Unidades Biologia Molecular, Universidad Autonoma de Madrid, Madrid, 28006, Spain

SOURCE: EMBO Journal (1998), 17(23), 7066-7077

CODEN: EMJODG; ISSN: 0261-4189

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The X gene product of the human hepatitis B virus (HBx) is a transcriptional activator of various viral and cellular genes. We recently have determined that the production of tumor necrosis factor- α (TNF- α) by **HBV**-infected hepatocytes is transcriptionally up-regulated by HBx, involving nuclear factor of activated T cells (NF-AT)-dependent activation of the TNF- α gene promoter. Here we show that HBx activates NF-AT by a **cyclosporin A**-sensitive mechanism involving dephosphorylation and nuclear translocation of the transcription factor. Luciferase gene expression assays demonstrated that HBx transactivates transcription through NF-AT-binding sites and activates a Gal4-NF-AT chimeric protein. DNA-protein interaction assays revealed that HBx induces the formation of NF-AT-containing DNA-binding complexes. Immunofluorescence anal. demonstrated that HBx induces the nuclear translocation of NF-AT, which can be blocked by the immunosuppressive drug **cyclosporin A**. Furthermore, immunoblot anal. showed that the HBx-induced activation and translocation of NF-AT are associated with its dephosphorylation. Thus, HBx may play a relevant role in the intrahepatic inflammatory processes by inducing locally the expression of cytokines that are regulated by NF-AT.

REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:872869 CAPLUS

DOCUMENT NUMBER: 123:337203

TITLE: In vitro activation of woodchuck lymphocytes measured by radiopurine incorporation and interleukin-2 production: Implications for modeling immunity and therapy in hepatitis B virus infection

AUTHOR(S): Cote, Paul J.; Gerin, John L.

CORPORATE SOURCE: Medical Center, Georgetown University, Rockville, MD, 20852, USA

SOURCE: Hepatology (Philadelphia) (1995), 22(3), 687-99

CODEN: HPTLD9; ISSN: 0270-9139

PUBLISHER: Saunders

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Cellular immune responses to hepatitis B virus (**HBV**) play an important role in the resolution of acute infection. They also influence the course of chronic infection and disease but are inadequate to completely clear the infection. Woodchuck hepatitis virus (WHV) infection of the woodchuck can provide a model to study these processes. Lymphocyte responses of woodchucks were assessed by in vitro proliferation and/or interleukin (IL)-2 assays using mitogen (ConA), cytokine (IL-2), superantigen (Staphylococcus aureus enterotoxin B [SEB]), MHC alloantigen (mixed lymphocyte reaction [MLR]), and viral antigens (woodchuck hepatitis virus core antigen [WHcAg] and woodchuck hepatitis virus surface antigen

[WHsAg]). ConA-stimulated woodchuck lymphocytes underwent cell division based on cell counting expts. and produced IL-2 as detected using an IL-2-dependent murine cell line but failed to incorporate sufficient tritiated thymidine; however, they did incorporate sufficient tritiated adenine and deoxyadenine to permit development of a meaningful proliferation assay. The IL-2 assay was sensitive and specific for detection of woodchuck IL-2 induced by mitogen, superantigen, and MLR. **Cyclosporin A** and FK506 specifically inhibited ConA- and SEB-induced IL-2 production by woodchuck lymphocytes. Pos. two-way MLRs were detected by IL-2 production and proliferation assay between woodchucks from different geog. regions, thus indicating divergence among MHC mols.; however, occasional neg. MLR reactions among indigenous pairs of woodchucks indicated that some woodchucks were mutually immunocompatible to some degree. The radioadenine proliferation assay was sensitive for detecting peripheral blood lymphocyte responses to WHcAg and WHsAg in adult woodchucks with recently resolved acute infections. The above systems should facilitate the design of adoptive therapy and liver transplantation expts. in the woodchuck, and also enable modeling of immune responses that promote and maintain chronic hepatitis B infection.

L3 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:710042 CAPLUS

DOCUMENT NUMBER: 123:132330

TITLE: Effect of immunosuppressive and antiviral agents on hepatitis B virus replication in vitro

AUTHOR(S): McMillan, Janine S.; Shaw, Tim; Angus, Peter W.; Locarnini, Stephen A.

CORPORATE SOURCE: Victorian Infectious Diseases Reference Laboratory, Fairfield Hospital, Fairfield, 3078, Australia

SOURCE: Hepatology (Philadelphia) (1995), 22(1), 36-43
CODEN: HPTLD9; ISSN: 0270-9139

PUBLISHER: Saunders

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Hepatitis B virus (HBV) DNA-transfected hepatoma cells were incubated with the immunosuppressive agents prednisolone, azathioprine, and **cyclosporin A** (CsA) and the antiviral agents ganciclovir and foscarnet to investigate the effects of these compds. on HBV replication. Prednisolone and azathioprine increased intracellular viral DNA and RNA levels approx. twofold and fourfold, resp. Treatment with CsA did not alter the levels of viral RNA or DNA. A combination of all three immunosuppressive agents increased the level of intracellular viral DNA eightfold, indicating an additive effect. Incubation of the cells in the presence of foscarnet decreased levels of both single-stranded and relaxed circular viral DNA, and in the presence of ganciclovir decreased the levels of relaxed circular viral DNA, predictable effects from their known mechanism of action. The stimulatory effect on viral replication induced by the combination of immunosuppressive agents was substantially inhibited by ganciclovir-foscarnet treatment. These observations could have implications for the management of recurrent HBV infection after liver transplantation.

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<u>#27</u>	Search HBV treatment and CsA	17:23:35	<u>37</u>

#26 Search **HBV treatment and RANTES**
#25 Search **HBV treatment and IL-8**
#24 Search **HBV treatment and chemokine**

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